

## **REMARKS**

Applicants respectfully request reconsideration of the present application in view of the foregoing amendments and these remarks.

### **I. Status of the Claims**

Claims 2 and 28 were cancelled previously. Claims 3, 9, 22, 25-27 and 29-36 are cancelled in this response without prejudice or disclaimer. Applicants reserve the right to file one or more continuing applications to pursue the subject matter of any cancelled claim.

Claims 1, 10 and 15-16 have been amended with support in the original claim 9 and in the specification, e.g., at page 3, last full paragraph; and at page 13, fourth paragraph. Claims 6 and 17-18 have been amended to correct dependency. Claims 37 and 38 have been added with exemplary support in the specification, at page 13, fourth paragraph.

Because no matter is introduced, Applicants respectfully request entry of this amendment. Upon entry, claims 1, 4-8, 10-21, 23-24, and 37-38 will be pending.

### **II. Claim Objections**

The Examiner objected to claims 25-27 and 29-36 for typographical errors. The claims in question are cancelled, mooting the objection.

### **III. Rejection of Claim under 35 U.S.C. § 112, second paragraph**

The Examiner rejected claim 19 because she deemed the phrase “the monovalent cation” to lack antecedent basis. Claim 15 has been amended to provide an antecedent basis for the phrase at issue. Therefore, withdrawal of the rejection is respectfully requested.

#### IV. Rejection of Claims under 35 U.S.C. § 102(b)

##### A. Sugiuchi

The Examiner rejected claims 25 and 27 for alleged anticipation by PCT Application WO 00/17388 by Sugiuchi, the English language equivalent of which is U.S. Patent No. 6,794,157.

Without acquiescing to the stated basis of the rejection, Applicants choose to expedite the prosecution by cancelling the claims at issue, thereby rendering the rejection moot.

##### B. JP 07294532

The Examiner rejected claims 1, 3-6, and 15-19 for alleged anticipation by JP 07294532 (“the ‘532 publication”). Claim 3 has been cancelled. Applicants respectfully traverse the rejection of the remaining claims.

According to the Examiner, the present invention and the cited art implicate using the same reagents, including a polyanion, a divalent cation and a monovalent cation. Thus, the examiner concludes that “the supernatant resulting after precipitation of LDL, VLDL and chylomicrons would inherently contain both HDL and small particle LDL therein” (Office Action at page 4, lines 4-9). The Examiner’s assessment overlooks the fact, however, that the reagents are used at different concentrations.

By way of background, the present invention is directed to methodology for quantifying or separating small particle LDL in a test sample. On page 1, second paragraph, Applicants’ specification teaches that small particle LDL, a subfraction of LDL, “is especially smaller in particle size among LDLs and higher in density than standard LDL.” As prescribed by claim 1, lipoproteins *other than small particle LDL and HDL* is removed by adding a separation agent comprising a polyanion, a divalent cation, and *a monovalent cation having a final concentration of less than 50 mmol/L*. Claim 15 recites that LDLs other than small particle LDL is precipitated by adding a separation agent comprising *a monovalent cation having a final concentration of less than 50 mmol/L*.

By contrast, the '532 publication describes:

- (i) a reagent for precipitating chylomicrons, VLDL and LDL contains 0.05-0.10 M (50-100 mmol/L) monovalent cation, which is at the minimum concentration to solubilize proteins other than lipoproteins (paragraph [0013]);
- (ii) a reagent for precipitating chylomicrons and VLDL contains 0.1-0.2 M (100-200 mmol/L) monovalent cation (paragraph [0014]); and
- (iii) a reagent for precipitating only chylomicrons contains 0.15-0.2 M (150-200 mmol/L) monovalent cation (paragraph [0015]).

Accordingly, one skilled in the art would conclude, based on the teachings of the '532 publication, that (a) the prior art does not teach a reagent having a monovalent cation at a concentration of *less than 50 mmol/L*, as claims 1 and 15 recite, and (b) different fractions of lipoprotein may be precipitated in the presence of a monovalent cation at different concentrations.

"[P]rior art which teaches a value or range that is very close to, but does not overlap or touch, the claimed range does not anticipate the claimed range." MPEP § 2131.03. Accordingly, the art of record here must fail to anticipate the claimed invention. Moreover, the Examiner is incorrect in assuming that the supernatant after precipitation would "inherently" (*necessarily*) contain the same fractions as in the prior art, because the monovalent cation is used at a different concentration. Accordingly, withdrawal of the anticipation rejection is warranted.

## V. Rejection of Claims under 35 U.S.C. § 103(a)

### A. JP 07294532

The Examiner rejected claims 7-9, 12-14 and 20-22 for alleged obviousness over JP 07294532. Claims 9 and 22 have been cancelled. Applicants respectfully traverse the rejection of the remaining claims.

Armed with the teachings of the '532 publication, one skilled in the art would not have found it obvious to add a reagent comprising a monovalent cation at a concentration of less than 50

mmol/L to a test sample, given the absence from the '532 publication of any suggestion concerning quantifying or separating small particle LDL.

Accordingly, claims 1 and 15 are non-obvious over the cited art, as are dependent claims 7-8, 12-14 and 20-21. Applicants respectfully request withdrawal of the rejection, therefore.

**B. JP 07294532 and Sugiuchi**

The Examiner rejected claims 10-11 and 23-24 for alleged obviousness over JP 07294532 in view of Sugiuchi. The Examiner also rejected claims 26 and 29 for alleged obviousness over Sugiuchi in view of JP 07294532. Claims 26 and 29 are cancelled. Applicants respectfully traverse the remaining ground of the rejection.

The '532 publication is discussed above. The Examiner cites Sugiuchi for the alleged teaching of PEG. According to the Examiner, "Sugiuchi teaches that PEG is a known aggregating agent for aggregating lipoproteins in a serum sample that acts equivalently to a polyanion such as dextran sulfate" (Office Action, page 6, lines 6-9).

The reagent of the '532 publication comprises a divalent cation and a monovalent cation, in addition to a polyanion. As the Examiner correctly characterized, Sugiuchi teaches that PEG acts equivalently to a polyanion, but there is no indication that PEG can replace a divalent cation or a monovalent cation. In fact, the working examples of Sugiuchi demonstrate that PEG is used in combination with a divalent metal salt to aggregate lipoprotein other than HDL.

By contrast, the claimed invention entails removing lipoproteins other than small particle LDL and HDL or precipitating LDLs other than small particle LDL by adding PEG *alone* to the test sample, as prescribed by claims 10 and 23. In other words, unlike the cited art, PEG is sufficient for the claimed methodology in the absence of a divalent cation or a monovalent cation. Therefore, the combined teachings of the prior art fail to render the claimed invention obvious and withdrawal of the rejection is respectfully requested.

C. Sugiuchi

The Examiner rejected claims 30-36 for alleged obviousness over Sugiuchi. Claims 30-36 are cancelled presently, however, and the rejection is rendered moot.

**CONCLUSION**

Applicants submit that this application is in condition for allowance, and they request an early indication to this effect. Examiner Wallenhorst is invited to contact the undersigned directly, should she feel that any issue warrants further consideration.

The Commissioner is hereby authorized to charge any additional fees, which may be required under 37 CFR §§ 1.16-1.17, and to credit any overpayment to Deposit Account No. 19-0741. Should no proper payment accompany this response, then the Commissioner is authorized to charge the unpaid amount to the same deposit account. If any extension is needed for timely acceptance of submitted papers, then Applicants hereby petition for such extension under 37 CFR §1.136 and authorize payment of the relevant fee(s) from the deposit account.

Respectfully submitted,

By 

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